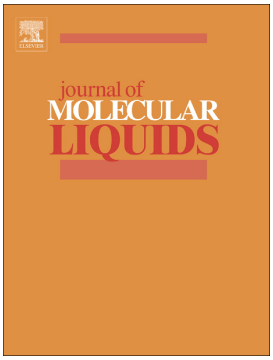

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Descriptors for adamantane and some of its derivatives

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ABSTRACT

Literature data on solubilities of adamantane in organic solvents have been used to obtain properties, or descriptors, of adamantane. There is much less data on substituted adamantanes but we have been able to obtain descriptors for some 40 substituted adamantanes. These descriptors can then be used to estimate a wide range of physicochemical, environmental and other properties of the adamantanes. For the first time, the water-solvent partition coefficient and the gas-solvent partition coefficient into a large range of solvents, can be estimated, the latter being equivalent to Henry's Law constants. A variety of other important properties can also be estimated. These include vapor pressures, enthalpies of vaporization and sublimation, partitions from air and from blood into biological tissues, and skin permeability from water. The descriptors themselves are not exceptional. Adamantane itself has a rather low dipolarity, zero hydrogen bond acidity and a very low hydrogen bond basicity, in common with other multicyclic aliphatic compounds. These lead to adamantane being a very hydrophobic compound, as is evident from our estimated water-octanol partition coefficient.

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1. Introduction

Adamantane was discovered as long ago as 1933 [1] and synthesized in 1942 [2]. Since then, there has been considerable interest in its properties, and a number of thermodynamic properties such as the vapor pressure and enthalpy of sublimation have been determined [3]. However, there is still a lack of information on physicochemical properties of adamantane and its derivatives. For example, solubilities in nonaqueous solvents are known for adamantane itself [4-6], but only for a few derivatives of adamantane. Adamantane and its derivatives are highly hydrophobic, but a common measure of hydrophobicity, the water-octanol partition coefficient, as log *Poct*, is known only for adamantane [7, 8], 1-aminoadamantane [9] and adamantan-1-ol [10]. We aim to use our method of obtaining properties or descriptors of adamantane from the available solubilities, and then show how these descriptors can be used to estimate a wide range of other physicochemical properties. Although there is only a limited amount of available data for substituted adamantanes we aim to obtain descriptors for a number of these compounds, and hence to be able to estimate physicochemical properties for these compounds as well.

2. Methodology

Our method makes use of the two linear free energy relationships, Eq. (1) and Eq. (2).

$$Log\ Ps = c + e\mathbf{E} + s\mathbf{S} + a\mathbf{A} + b\mathbf{B} + v\mathbf{V} \quad (1)$$

$$Log\ Ks = c + e\mathbf{E} + s\mathbf{S} + a\mathbf{A} + b\mathbf{B} + l\mathbf{L} \quad (2)$$

Eq. (1) is used when the dependent variable, log *Ps*, refers to a water-solvent partition coefficient for a series of solutes in a given system. Eq. (2) is used when log *Ks* refers to a gas to solvent partition, where *Ks* is the gas to solvent partition coefficient.

The independent variables in Eqs. (1) and (2) are solute descriptors as follows [11-15]: **E** is the solute excess molar refractivity in units of $(cm^3\ mol^{-1})/10$, *S* is the solute dipolarity / polarizability, **A** and **B** are the overall or summation hydrogen bond acidity and basicity, **V** is the McGowan characteristic volume [16] in units of $(cm^3\ mol^{-1})/100$ and **L** is the logarithm of the gas-hexadecane partition coefficient, at 298.15 K. The coefficients in Eqs. (1) and (2) are obtained by multiple linear regression analysis, and serve to characterize the system under consideration.

In order to apply Eq. (1) or Eq. (2), values of the dependent variable are needed. The most direct source is the water-solvent partition coefficient. These can be obtained directly and can also be obtained indirectly, from solubilities in mol dm^{-3}, in water, *Cw*, and a given (dry) solvent, *Cs*, through Eq. (3).

$$\text{Log } Ps = \log Cs - \log Cw \quad (3)$$

If a value of log *Cw* is unavailable, it can be taken as another variable to be determined. We can greatly increase the number of dependent variables by converting every log *Ps* into a corresponding log *Ks* value, through Eq. (4). Now log *Kw* itself is another variable to be determined.

$$\text{Log } Ps = \log Ks - \log Kw \quad (4)$$

Then for a given compound we have a number of log *Ps* and log *Ks* values as the dependent variable with the corresponding equations, Eq. (1) and Eq. (2), for which the coefficients are known, and which defines a set of simultaneous equations. The unknowns are the compound descriptors **E**, **S, A**, **B**, **V**, **L,** and log *Kw*, that can be obtained as the solution of the set of simultaneous equations that can be solved by trial-and-error to give a 'best-fit' solution, using the Microsoft 'Solver' add-on. Note that partition into solvents can refer to 'dry' solvents when obtained through Eq. 3, but to 'wet' solvents when obtained by direct partition measurements. The coefficients in Eq. (1) and Eq. (2) that we shall use are in Table 1 and Table 2.

Table 1.

Coefficients in Eq. (1) for water-solvent partitions as log *P*s.

Solvent	Coefficients					
	c	*e*	*s*	*a*	*b*	*v*
Methanol	0.276	0.334	-0.714	0.243	-3.320	3.549
Ethanol	0.222	0.471	-1.035	0.326	-3.596	3.857
Propan-1-ol	0.139	0.405	-1.029	0.247	-3.767	3.986
Butan-1-ol	0.165	0.401	-1.011	0.056	-3.958	4.044
Pentan-1-ol	0.150	0.536	-1.229	0.141	-3.864	4.077
Hexan-1-ol	0.115	0.492	-1.164	0.054	-3.971	4.131
Heptan-1-ol	0.035	0.398	-1.063	0.002	-4.342	4.317
Nonan-1-ol	-0.031	0.540	-1.232	0.022	-4.288	4.249
Decan-1-ol	-0.058	0.616	-1.319	0.026	-4.153	4.279
Propan-2-ol	0.099	0.344	-1.049	0.406	-3.827	4.033
2-Methylpropan-1-ol	0.188	0.354	-1.127	0.016	-3.568	3.968
2-Methylpropan-2-ol	0.211	0.171	-0.947	0.331	-4.085	4.109
2-Methylbutan-2-ol	0.177	0.316	-1.125	0.306	-4.112	4.178
Dioxane	0.123	0.747	-0.033	-0.582	-4.810	4.110
Tetrahydrofuran	0.223	0.363	-0.384	-0.238	-4.932	4.450
Cyclohexanone	0.077	0.249	0.028	-0.891	-4.917	4.283
Dichloromethane	0.319	0.102	-0.187	-3.058	-4.090	4.324
Tetrachloromethane	0.199	0.523	-1.159	-3.560	-4.594	4.616
Pentane	0.369	0.386	-1.568	-3.535	-5.215	4.514
Hexane	0.333	0.560	-1.710	-3.578	-4.939	4.463
Heptane	0.297	0.634	-1.755	-3.571	-4.946	4.488
Octane	0.231	0.738	-1.840	-3.685	-4.907	4.502
Decane	0.186	0.722	-1.741	-3.449	-4.970	4.476
Undecane	0.058	0.603	-1.661	-3.421	-5.120	4.619
Hexadecane	0.087	0.667	-1.617	-3.587	-4.869	4.433
Gas-water	-0.994	0.577	2.549	3.813	4.841	-0.869
Cyclohexane	0.159	0.784	-1.678	-3.740	-4.929	4.577
Benzene	0.142	0.464	-0.588	-3.099	-4.625	4.491
Toluene	0.125	0.431	-0.644	-3.002	-4.748	4.524
o-Xylene	0.083	0.518	-0.813	-2.884	-4.821	4.559
m-Xylene	0.122	0.377	-0.603	-2.981	-4.961	4.535
p-Xylene	0.166	0.477	-0.812	-2.939	-4.874	4.532
Octan-1-ol, wet	0.088	0.562	-1.054	0.034	-3.460	3.814

Table 2.

Coefficients in Eq. (2) for gas-solvent partitions as log *Ks*.

Solvent	Coefficients					
	c	*e*	*s*	*a*	*b*	*l*
Methanol	-0.039	-0.338	1.317	3.826	1.396	0.773
Ethanol	0.017	-0.232	0.867	3.894	1.192	0.846
Propan-1-ol	-0.042	-0.246	0.749	3.888	1.076	0.874
Butan-1-ol	-0.004	-0.285	0.768	3.705	0.879	0.890
Pentan-1-ol	-0.002	-0.161	0.535	3.778	0.960	0.900
Hexan-1-ol	-0.014	-0.205	0.583	3.621	0.891	0.913
Heptan-1-ol	-0.056	-0.216	0.554	3.596	0.803	0.933
Nonan-1-ol	-0.105	-0.146	0.431	3.532	0.694	0.954
Decan-1-ol	-0.139	-0.090	0.356	3.547	0.727	0.958
Propan-2-ol	-0.048	-0.324	0.713	4.026	1.055	0.884
2-Methylpropan-1-ol	-0.003	-0.357	0.699	3.895	1.247	0.881
2-Methylpropan-2-ol	0.053	-0.443	0.699	4.026	0.882	0.907
2-Methylbutan-2-ol	0.014	-0.435	0.573	3.965	0.811	0.943
Dioxane	-0.034	-0.389	1.724	2.989	0.000	0.866
Tetrahydrofuran	0.193	-0.391	1.244	3.256	0.000	0.994
Cyclohexanone	-0.052	-0.445	1.716	2.758	0.000	0.948
Dichloromethane	0.192	-0.572	1.492	0.460	0.847	0.965
Tetrachloromethane	0.217	-0.435	0.554	0.000	0.000	1.069
Pentane	0.351	0.000	0.000	0.000	0.000	0.953
Hexane	0.320	0.000	0.000	0.000	0.000	0.945
Heptane	0.284	0.000	0.000	0.000	0.000	0.950
Octane	0.219	0.000	0.000	0.000	0.000	0.960
Decane	0.159	0.000	0.000	0.000	0.000	0.972
Undecane	0.113	0.000	0.000	0.000	0.000	0.971
Hexadecane	0.000	0.000	0.000	0.000	0.000	1.000
Gas-water	-1.271	0.822	2.743	3.904	4.814	-0.213
Cyclohexane	0.163	-0.110	0.000	0.000	0.000	1.013
Benzene	0.107	-0.313	1.053	0.457	0.169	1.020
Toluene	0.085	-0.400	1.063	0.501	0.154	1.011
o-Xylene	0.064	-0.296	0.934	0.647	0.000	1.010
m-Xylene	0.071	-0.423	1.068	0.552	0.000	1.014
p-Xylene	0.113	-0.302	0.826	0.651	0.000	1.010
Octan-1-ol, wet	-0.222	0.088	0.701	3.473	1.477	0.851

3. Results

The solubility of adamantane in a large number of solvents has been determined [4-6], and these can be used to deduce values of log *Ps* through Eq. 3 with log *Cw* as an extra

unknown descriptor to be determined, and then to deduce values of log *Ks* through Eq. (4) with log *Kw* as an extra unknown descriptor. We also have an experimental value of log *Poct* [7, 8], and an experimental value of the **L**-descriptor [17], giving a total number of 66 equations. It is useful to estimate or to calculate as many descriptors as possible, and so to reduce the number to be obtained from the set of equations. The **E**-descriptor can be obtained from the refractive index of a liquid compound at 293.15 K. If the compound is a solid, then a refractive index can be calculated, or the **E**-value can itself be calculated. From a calculated refractive index [18], **E** = 0.756, and the ADME [19] software gives **E** = 0.66. Although adamantane is a solid, several alkyl adamantanes are liquid at 293.15 K, and their refractive indices have been determined [20], leading to **E** = 0.64 for 1-ethyladamantane and **E** = 0.70 for 2-ethyladamantane. We take **E** = 0.70 for adamantane, but note that changes in **E** have little effect on the overall statistics. The **V**-descriptor can easily be calculated [11, 16] as **V** = 1.1918, and so we have as unknowns **S**, **A, B**, **L**, log *Kw* and log *Cw* to be obtained from the solution of 66 simultaneous equations. Our trial-and-error method yielded the descriptors given in Table 3, with log *Cw* as -5.402. The observed and calculated dependent variables are in Table 4, with an average error, *AE*, of 0.001 and a standard deviation, *SD*, of 0.127 log units.

Table 3.

Obtained descriptors for adamantane and derivatives of adamantane

Compound	**E**	**S**	**A**	**B**	**V**	**L**	log *Kw*
Adamantane	0.70	0.37	0.00	0.08	1.1918	4.797	-0.14
1-Methyladamantane	0.65	0.36	0.00	0.09	1.3327	4.995	-0.39
2-Methyladamantane	0.70	0.37	0.00	0.08	1.3327	5.177	-0.41
1,3-Dimethyladamantane	0.60	0.16	0.00	0.08	1.4736	5.294	-1.11
cis-1,4-Dimethyladamantane	0.61	0.20	0.00	0.08	1.4736	5.505	-1.02
trans-1,4-Dimethyladamantane	0.61	0.20	0.00	0.08	1.4763	5.525	-1.02
1-Ethyladamantane	0.64	0.36	0.00	0.08	1.4763	5.711	-0.60
2-Ethyladamantane	0.70	0.35	0.00	0.08	1.4736	5.845	-0.59
1-Propyladamantane	0.67	0.30	0.00	0.08	1.6145	6.295	-0.86
2-Propyladamantane	0.69	0.31	0.00	0.08	1.6145	6.261	-0.82
1-Ethyl-3-methyladamantane	0.59	0.18	0.00	0.08	1.6145	5.990	-1.20
cis-1,3,4-Trimethyladamantane	0.59	0.18	0.00	0.08	1.6145	5.725	-1.18
trans-1,3,4-Trimethyladamantane	0.59	0.18	0.00	0.08	1.6145	5.721	-1.17
1,3,5-Trimethyladamantane	0.59	0.18	0.00	0.08	1.6145	5.312	-1.12
1,3,6-Trimethyladamantane	0.59	0.22	0.00	0.08	1.6145	5.555	-1.15
1,2,5,7-Tetramethyladamantane	0.56	0.16	0.00	0.08	1.7554	5.729	-1.32
1,3,5,7-Tetamethyladamantane	0.56	0.14	0.00	0.08	1.7554	5.310	-1.34

1-Butyladamantane	0.64	0.21	0.00	0.08	1.7554	6.884	-1.23
2-Butyladamantane	0.69	0.20	0.00	0.08	1.7554	6.929	-1.22
1-sec-Butyladamantane	0.62	0.30	0.00	0.08	1.7554	6.895	-1.01
1-tert-Butyladamantane	0.60	0.30	0.00	0.08	1.7554	6.891	-1.03
2-Isobutyladamantane	0.67	0.23	0.00	0.08	1.7554	6.850	-1.16
1-Isopropyladamantane	0.67	0.33	0.00	0.08	1.6145	6.348	-0.78
2-Isopropyladamantane	0.65	0.27	0.00	0.08	1.6140	6.326	-0.95
1,3-Diethyladamantane	0.60	0.26	0.00	0.08	1.7554	6.620	-1.10
1-Ethyl-3,5-dimethyladamantane	0.58	0.18	0.00	0.08	1.7554	6.682	-1.30
1-Chloroadamantane	0.88	0.78	0.00	0.10	1.3142	5.539	0.87
2-Chloroadamantane	0.88	0.85	0.00	0.10	1.3142	5.490	0.93
1,3-Dichloroadamantane	0.85	0.99	0.00	0.10	1.4366	6.120	1.29
1,3,5-Trichloroadamantane	0.92	1.22	0.00	0.10	1.5590	6.736	1.83
1-Bromoadamantane	1.05	0.89	0.00	0.10	1.3668	5.602	1.25
2-Bromoadamantane	1.05	0.96	0.00	0.10	1.3668	5.720	1.42
1,3-Dibromoadamantane	1.20	1.25	0.00	0.10	1.5418	6.367	2.15
1,3,5-Tribromoadamantane	1.47	1.32	0.00	0.10	1.7168	7.649	2.31
2-Adamantanone	0.88	1.13	0.00	0.47	1.2075	5.503	3.63
1-Aminoadamantane	0.78	0.64	0.12	0.72	1.2916	5.283	3.89
1-Adamantanol	0.91	0.99	0.30	0.63	1.2505	5.623	5.18
2-Adamantanol	0.91	1.13	0.30	0.59	1.2505	5.771	5.34
1-Cyanoadamantane	0.90	1.17	0.00	0.40	1.3465	6.080	3.29
2-Cyanoadamantane	0.87	1.10	0.00	0.37	1.3465	6.019	2.95
1-Nitroadamantane	0.92	1.05	0.00	0.33	1.3660	6.087	2.64
2-Nitroadamantane	0.92	1.14	0.00	0.35	1.3600	6.152	2.97

Table 4.

Calculated and observed values of water-solvent partition, as log *Ps*, gas-solvent partition, as log *Ks*, and solubilities, as log *Cs*, for adamantane.

Solvent	Log *Ps calc*	Log *Ps obs*	Log *Cs*	Ref [a]
Methanol	4.210	4.067	-1.335	4
Ethanol	4.478	4.204	-1.198	4
Propan-1-ol	4.491	4.347	-1.055	4
Butan-1-ol	4.575	4.429	-0.973	4
Pentan-1-ol	4.620	4.695	-0.707	4
Hexan-1-ol	4.634	4.657	-0.745	4
Heptan-1-ol	4.718	4.543	-0.859	4
Nonan-1-ol	4.612	4.485	-0.917	4
Decan-1-ol	4.653	4.440	-0.962	4
Propan-2-ol	4.452	4.337	-1.065	4
2-Methylpropan-1-ol	4.462	4.346	-1.056	4
2-Methylpropan-2-ol	4.551	4.558	-0.844	4
2-Methylbutan-2-ol	4.632	4.679	-0.723	4
Dioxane	4.867	4.952	-0.450	4

Tetrahydrofuran	5.244	5.348	-0.054	5
Cyclohexanone	4.973	4.800	-0.602	4
Dichloromethane	5.147	5.220	-0.182	3
Tetrachloromethane	5.272	5.345	0.101	3
Pentane	5.022	5.179	-0.223	5
Hexane	5.016	5.028	-0.374	5
Heptane	5.045	5.165	-0.237	5
Octane	5.040	5.157	-0.245	5
Decane	4.984	5.118	-0.284	5
Undecane	4.961	5.068	-0.334	5
Hexadecane	4.849	4.914		17
Gas-water	-0.295	-0.144		
Cyclohexane	5.147	5.253	-0.149	5
Benzene	5.232	5.295	-0.107	5
Toluene	5.200	5.245	-0.157	5
o-Xylene	5.193	5.235	-0.167	5
m-Xylene	5.171	5.240	-0.162	5
p-Xylene	5.211	5.226	-0.173	5
Octan-1-ol, wet	4.360	4.240		7

	Log *Ks calc*	Log *Ks obs*
Methanol	4.032	3.923
Ethanol	4.329	4.060
Propan-1-ol	4.342	4.203
Butan1-ol	4.429	4.285
Pentan-1-ol	4.478	4.551
Hexan-1-ol	4.509	4.513
Heptan-1-ol	4.538	4.399
Nonan-1-ol	4.582	4.485
Decan-1-ol	4.584	4.296
Propan-2-ol	4.314	4.193
2-Methylpropan-1-ol	4.332	4.346
2-Methylpropan-2-ol	4.423	4.558
2-Methylbutan-2-ol	4.510	4.679
Dioxane	4.755	4.808
Tetrahydrofuran	5.148	5.204
Cyclohexanone	4.819	4.656
Dichloromethane	5.041	5.076
Tetrachloromethane	5.246	5.201
Pentane	4.923	5.035
Hexane	4.853	4.884
Heptane	4.841	5.021
Octane	4.824	5.013

Decane	4.822	4.974
Undecane	4.771	4.924
Hexadecane	4.797	4.770
Gas-water	-0.317	-0.144
Cyclohexane	4.946	5.109
Benzene	5.184	5.151
Toluene	5.061	5.101
o-Xylene	5.048	5.091
m-Xylene	5.034	5.096
p-Xylene	5.057	5.082
Gas-wet octanol	4.296	4.096

[a] Reference for the solubilities

As mentioned before, solubilities in organic solvents are known only for a few simple derivatives of adamantane, so calculations on the lines of those for adamantane are generally not possible. However, gas-chromatographic, GC, retention indices for derivatives of adamantane have been reported [20-24], and we have derived equations on the lines of Eq. 2 for these sets of data, see Table 5. The known [20] refractive indices for several alkyladamantanes yield values of **E**, and these can be used to estimate, with reasonable accuracy, **E**-values for other alkyladamantanes. Values of **B** remain almost the same for alkyl derivatives of hydrocarbons, for example cycloalkenes and alkylcycloalkenes, and so we can take **B** = 0.08 for simple alkyl derivatives of adamantane. **V** can be calculated, **A** = 0, and so we have only **S** and **L** to deduce from the GC equations; log *Kw* is automatically calculated. Descriptors for alkyladamantanes obtained in this way are in Table 3. GC data are also available [25] for halo substituted adamantanes, and we adopted a similar strategy to that for the alkyladamantanes to obtain the descriptors in Table 3.

There are a number of other substituted adamantanes for which data are available. GC data [26] and the vapor pressure at 298 K [3] are known for 2-adamantanone; we have calculated values of **E** and **V,** as before, and used this data to obtain the descriptors in Table 3. In the case of the adamantanols, log *Poct* is known [10], GLC data are available [26], as are also the vapor pressures [27]. **E** and **V** were calculated as before. Results for 1-adamantanol and 2-adamantanol are in Table 3.

Water-solvent partition coefficients into octanol, trichloromethane and heptane have been determined for 1-aminoadamantane [10], GC retention data [22] and the vapor pressure [28] are known, and so there is a reasonable amount of experimental data available. We take **E** = 0.78 by comparison to adamantane and known values for amines and **V** is calculated as 1.2916. We have fourteen simultaneous equations that were solved to give the descriptors in Table 3, with an *SD* of 0.104 log units.

Table 5.

Coefficients in Eq. (2) for GC retention indices

GLC phase	*c*	*e*	*s*	*a*	*b*	*l*
Apiezon [21]	94.9	72.4	313.3	0.0	0.0	194.6
Carbowax 20M [21]	86.7	284.5	0.0	0.0	0.0	195.7
OV 275 [21]	71.0	367.1	0.0	0.0	0.0	198.2
Apiezon [22]	76.5	55.8	312.0	0.0	0.0	197.0
Apiezon [20]	111.5	0.0	318.8	0.0	547.1	192.2
SE-30 [20]	114.9	0.0	263.6	0.0	0.0	191.7
HP-5MS [23]	72.7	0.0	93.9	0.0	0.0	197.0
HP-5MS [24]	43.6	0.0	116.0	0.0	0.0	201.0
SE-30 [25]	73.1	17.1	190.0	0.0	0.0	198.0
PMS [25]	72.6	38.8	197.0	0.0	0.0	198.0
OV-275 [25]	74.5	118.0	426.0	0.0	0.0	198.0
CW-20M [25]	63.1	35.7	695.0	0.0	0.0	199.0
DB-1 [26][6]	116.9	-244.2	167.6	212.6	82.4	191.6

In the case of 1-cyanoadamantane and 2-cyanoadamantane, only vapor pressure measurements [29, 30] are available, but we can obtain values of **E** from an ACD calculated refractive index [18], or from the ACD ADME software [19]. The latter calculates all the descriptors, not only **E**, and is a very useful aid in obtaining descriptors when little experimental data is available. For 1-cyanoadamantane we took **E** = 0.90 [18, 19] and we calculate **V** = 1.3465. **A** is zero, and the descriptors we estimate are in Table 3. Calculations for 2-cyanoadamantane are essentially the same except that **E** = 0.87 [18,19].

Our analysis of data for 1-nitroadamantane and 2-nitroadamantane follows that for the cyanoadamantanes. Vapor pressures are known [31], we estimated **E** as before [18,19], we calculated **V** as 1.3660 and **A** is zero. The various descriptors are in Table 3.

4. Discussion

For adamantane itself, we collected enough experimental data to be able to construct a set of no less than 66 simultaneous equations from which to derive descriptors. These descriptors are not in any way exceptional. **E** is quite large at 0.70, but comparable to **E** for cis-decahydronaphthalene, 0.544, quadricyclane, 0.548 and cholestane, 0.766. **S** and **B** are small, and **A** is zero, all as expected for a polycyclic aliphatic hydrocarbon. It is particularly important to obtain a definitive set of descriptors for adamantane, because these then form a benchmark in the determination of descriptors for simple substituted adamantanes. These obtained descriptors can be compared to descriptors for substituted alkanes and cycloalkanes. Again, there is nothing unusual and so we regard the set of descriptors in Table 3 as forming a reasonably coherent data set.

Once descriptors are available, they can be used to estimate a wide range of physicochemical [32] and environmental properties [14, 33, 34] including, of course, water-solvent partitions and gas-water partitions for all the systems listed in Table 1 and Table 2. We can illustrate this through calculations of log *Poct*, the usual measure of compound hydrophobicity. The descriptors in Table 3 and the equation for log *Poct* in Table 1 under 'Octan-1-ol, wet' are all that is needed for the calculations. We can compare our calculations with the (few) experimental values, and with values calculated by three common methods, ClogP from BioLoom [10], the ACD method [18], and the US Environmental Protection Agency (EPI) suite TM [35]. The ACD and the EPI calculated values are easily available through 'Chem Spider' [36]. In addition to these three general methods for the estimation of log *Poct*, there are two methods specific to adamantanes [22, 37, 38] that have been developed. These calculated values are in Table 6, together with the three observed values. It can be seen straight away that the calculated values of Kurbatova et al. [22, 37] and of Bayat and Zanoozi [38] are of little value. Comparison with the three experimental values in Table 6 shows that their calculated

values are too low by 1.19 [22, 37] and 0.80 [38] log units on average. Of the other calculations, our method and the ACD method yield the best comparisons with the experimental values.

Table 6.

Experimental and calculated values of the water-octanol partition coefficient, as log *Poct*, for adamantane and derivatives.

Compound	Exp	Calculated					
		This work	ClogP	ACD	EPI	[22, 38]	[38]
Adamantane	4.24 [7,8]	4.36	5.02	4.22	3.04	2.69	2.82
1-Methyladamantane		4.85	5.54	4.70	4.39	3.13	3.01
2-Methyladamantane		4.90	5.54	4.71	4.35	3.02	3.22
1,3-Dimethyladamantane		5.60	6.06	5.18	4.84	3.56	3.51
cis-1,4-Dimethyladamantane		5.54	6.06	5.19	4.81		
trans-1,4-Dimethyladamantane		5.56	6.06	5.19	4.81		
1--Ethyladamantane		5.41	6.06	5.18	4.84	3.52	3.43
2--Ethyladamantane		5.43	6.06	5.18	4.84	3.42	3.54
1-Propyladamantane		6.03	6.60	5.76	5.37	3.92	3.80
2-Propyladamantane		6.03	6.60	5.76	5.37	3.81	
1-Ethyl-3-methyladamantane		6.11	6.59	5.71	5.34	3.95	3.92
cis-1,3,4-Trimethyladamantane		6.11	6.58	5.67	5.26		
trans-1,3,4-Trimethyladamantane		6.11	6.58	5.67	5.26		
1,3,5-Trimethyladamantane		6.11	6.06	5.18	4.84	3.99	
1,3,6-Trimethyladamantane		6.11	6.06	5.18	4.84		
1,2,5,7-Tetramethyladamantane		6.65	7.10	6.14	5.75		
1,3,5,7-Tetamethyladamantane		6.67	7.10	6.14	5.75	4.42	4.86
1-Butyladamantane		6.64	7.13	6.30	5.86	4.31	4.21
2-Butyladamantane		6.68	7.13	6.31	5.83	4.21	4.08
1-sec-Butyladamantane		6.54	7.00	6.11	5.79	4.25	4.12
1-tert-Butyladamantane		6.53	6.87	5.93	5.75	4.29	4.19
2-Isobutyladamantane		6.64	7.00	6.12	5.75	4.15	4.20
1-Isopropyladamantane		6.00	6.47	5.58	5.30	3.85	3.83
2-Isopropyladamantane		6.05	6.47	5.59	5.26	3.75	3.98
1,3-Diethyladamantane		6.57	7.12	6.24	5.83	4.35	4.34
1-Ethyl-3,5-dimethyladamantane		6.64	7.11	6.19	5.79	4.35	
1-Chloroadamantane		4.43	4.86	3.86	4.15	2.60	2.76
2-Chloroadamantane		4.35	4.86	3.87	4.12		3.41
1,3-Dichloroadamantane		4.65	4.69	3.44	4.37		
1,3,5-Trichloroadamantane		4.92	4.52	3.00	4.59		
1-Bromoadamantane		4.61	4.99	4.03	4.24	2.66	3.36
2-Bromoadamantane		4.53	4.99	4.04	4.21		

1,3-Dibromoadamantane		4.98	4.97	3.98	4.55		
1,3,5-Tribromoadamantane		5.72	4.94	4.08	4.85		
2-Adamantanone		2.37	2.53	1.60	2.59	2.31	2.71
1-Aminoadamantane	2.44 [10]	2.29	2.00	2.22	2.43	1.11	1.63
1-Adamantanol	2.14 [10]	2.16	1.89	2.16	2.43	1.45	1.96
2-Adamantanol		2.15	2.93	2.18	2.40		
1-Cyanoadamantane		3.11	3.36	2.44	2.92		
2-Cyanoadamantane		3.27	3.36	2.45	2.89		
1-Nitroadamantane		3.57	3.41	2.70	1.42		
2-Nitroadamantane		3.40	3.41	2.70	1.42		

An important physicochemical and environmental property is the Henry's law constant, which can be very difficult to obtain experimentally. An often-used method is to determine the saturated vapor pressure and the water solubility of a compound, both at 298.15 K, which together yields the Henry's law constant or the gas to water partition coefficient, *Kw*, which is the inverse of Henry's law constant, with due regard to units. Inspection of the properties of adamantane shows how difficult is this method; the vapor pressure is very small, at 1.8×10^{-4} atm at 298.15 K [39] and we estimate the solubility in water as 4.0×10^{-6} mol dm^{-3} at 298.15 K. These lead to an estimated value for log *Kw* of -0.27, actually in quite good agreement with our value of -0.14 (Table 3). The most comprehensive collection of Henry's law constants [40] does not include adamantane and so our values for adamantane and its derivatives represent the first such determinations. Because values of log *Kw* are automatically determined by our descriptor method, see Table 3, this represents a very valuable and useful method [15] of obtaining log *Kw* and hence Henry's law constants.

Other properties that can be estimated are vapor pressures [41] and enthalpies of vaporization and sublimation [42, 43], the important partitions from air to biological tissues and from blood to biological tissues [44, 45], and skin permeation [44, 45]. We conclude that our descriptor method can be applied to adamantane and its derivatives, just as it can to organic and organometallic compounds in general.

5. Conclusions

We have used experimental data on solubilities of adamantane to obtain a set of 66 simultaneous equations that can be solved to yield descriptors for adamantane. We regard

these descriptors as firmly based, and so they can be used as a benchmark in the determination of descriptors for alkyladamantanes for which we have limited data. We have also determined descriptors for a number of other substituted adamantanes. These descriptors are not exceptional and are quite commensurate with descriptors for other polycyclic aliphatic compounds. The descriptors for the adamantanes can be used to estimate a large number of physicochemical and other properties, including the water-octanol partition coefficient which is a useful measure of hydrophobicity. These estimations use equations that we have previously developed, and can be calculated by simple arithmetic.

Conflicts of interest

There are no conflicts of interest to declare

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This manuscript or a very similar manuscript has not been published, nor is under consideration by any other journal.

There are no conflicts of interest to report

- Descriptors determined for 40 substituted adamantanes
- Used to predict solubilities and partition coefficients
- Used to predict thermodynamic quantities
- Descriptors not unusual for multi-cyclic compounds.